USE OF META-ANALYSIS: EPIDEMIOLOGIC STUDIES ON ETS AND LUNG CANCER

Introduction

The statistical procedure of meta-analysis treats the results of individual studies as individual data points in an overall analysis. It has been used effectively in combining the results of randomized, controlled clinical trials of pharmaceuticals. Such studies are eminently comparable because their methodologies and study populations are very similar.

More recently, meta-analysis has been used to analyze the results of epidemiologic studies, that is, to calculate an overall relative risk as a weighted average of the relative risks of many studies. Because of the inherent differences in study design, methodology, and sample population, especially in the case of epidemiologic studies on ETS and lung cancer, questions have been raised regarding the appropriateness of using this procedure to analyze epidemiologic data. However, meta-analysis is still being used; most recently, the U.S. Environmental Protection Agency (EPA) used a meta-analysis to calculate an estimated overall relative risk for lung cancer related to exposure to environmental tobacco smoke (ETS).[1]

The EPA meta-analysis is not the first in this area. The risk estimates calculated by several other meta-analyses are given in Table 1 for comparison.[2-8]

In addition to its meta-analysis on United States ETS-lung cancer studies, the recent paper by Fleiss and Gross (1991) presents a detailed criticism of the meta-analytical method, particularly as applied to the ETS literature.[8] This is a thorough review paper and a useful reference. Some relevant quotations follow:

> [T]he authors of the NRC report appear not to have followed the major guidelines proposed by Sacks, et al. For example, they did not provide a formal protocol for the meta-analysis, nor, apparently, did they give any consideration to the possibility of heterogeneous ORs across the several studies. (p. 134)
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> Furthermore, the question comes to mind whether the existing epidemiological studies of a possible association between exposure to ETS and the incidence of lung cancer in non-smokers are of adequate quality. Indeed, there is the question whether any of these studies meets even minimal standards of quality. (pp. 134-135)
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> There are many reasons for restricting attention to American studies of whether there is an elevated risk of lung cancer to non-smokers exposed to ETS relative to non-smokers not so exposed. One is that this is the population to whom policy decisions will apply and on whom those decisions should be based. (p. 135)
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> Odds ratios from studies in other countries, on the other hand, are derived from distributions that may differ markedly from those in the U.S., and thus the ORs themselves may not be relevant to the American experience. Genetic and lifestyle differences between the U.S. population and the populations studied elsewhere (mainly in east Asia) also argue for a meta-analysis only of U.S. studies. (p. 135)

> [U]ncritical use of meta-analysis can and does lead to unsubstantiated conclusions. Only when all the issues that we have discussed are considered and possibly accounted for is it possible to apply meta-analysis so that the overall result is scientifically valid. (p. 137)
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> It is very unlikely that the biases present in the epidemiological studies of the possible association between exposure to ETS and the risk of lung cancer can ever be removed. The meta-analysis performed by the NRC must either be completely discounted or, as Stein concluded so succinctly in another context, considered a mere 'computational exercise.' (p. 137)

(An editorial comment on this paper by Spitzer is also included.[9])

Copies of some of the referenced articles are included at Tabs 1-4. They are highlighted in yellow for useful information, and in blue for adverse information.

Table 1. Results of Meta-Analyses of Epidemiologic Studies of Spousal Smoking and Female Lung Cancer

Meta-Analysis	Summary Risk Estimate	Studies Included
Wald, et al., 1986	1.35 (95% CI 1.19-1.54)	13; 10 case-control, 3 cohort
NRC, 1986	1.32 (95% CI 1.16-1.51)	13; 10 case-control, 3 cohort
Blot and Fraumeni, 1986	1.3 (95% CI 1.1-1.5)	12; 10 case-control, 2 cohort
Wells, 1988	1.44 (95% CI 1.26-1.66)	17; 14 case-control, 3 cohort
EPA, 1990	1.41 (95% CI 1.26-1.57)	22; 19 case-control, 3 cohort
	1.25 (95% CI 1.03-1.52)	8 U.S. studies; 7 case-control, 1 cohort
Letzel and Überla, 1990	1.118 1.076	12; 10 case-control, 2 cohort 11; 9 case-control (Trichopoulos excluded), 2 cohort
Fleiss and Gross, 1991	1.12 (95% CI 0.95-1.30)	9 U.S. studies; 8 case-control, 1 cohort
Layard and LeVois, 1991 (unpublished)	1.08 (95% CI 0.96-1.22)	26; 23 case-control, 3 cohort

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REFERENCES

1. United States Environmental Protection Agency, "Health Effects of Passive Smoking: Assessment of Lung Cancer in Adults and Respiratory Disorders in Children," (Review Draft) EPA/600/6-90/006A, May, 1990.

2. Wald, N.J., Nanchahal, K., Thompson, S.G. and Cuckle, H.S., "Does Breathing Other People's Tobacco Smoke Cause Lung Cancer?," British Medical Journal 293: 1217-1222, 1986.

3. National Research Council, Environmental Tobacco Smoke: Measuring Exposure and Assessing Health Effects (Washington: National Academy Press, 1986).

4. Blot, W.J. and Fraumeni, J.F., "Passive Smoking and Lung Cancer," Journal of the National Cancer Institute 77(5): 993-1000, 1986.

5. Wells, A.J., "An Estimate of Adult Mortality in the United States from Passive Smoking," Environment International 14: 249-265, 1988.

6. Letzel, H. and Überla, K., "Meta-Analyses on Passive Smoking and Lung Cancer," Indoor Air Quality, ed. H. Kasuga (Berlin, Heidelberg: Springer-Verlag, 1990): 316-322.

7. Layard, M.W. and LeVois, M.E., Letter to Dr. Donald G. Barnes, Director of the Science Advisory Board, United States Environmental Protection Agency, April 9, 1991.

8. Fleiss, J.L. and Gross, A.J., "Meta-Analysis in Epidemiology, with Special Reference to Studies of the Association Between Exposure to Environmental Tobacco Smoke and Lung Cancer: A Critique," Journal of Clinical Epidemiology 44(2): 127-139, 1991.

9. Spitzer, W.O., "Meta-Meta-Analysis: Unanswered Questions About Aggregating Data," Journal of Clinical Epidemiology 44(2): 103-107, 1991.